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SCIENCE

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Joint Winners Half the Nobel Prize in Chemistry

Research and Medical Practice

Ernest W. Goodpasture

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SCIENCE

Vol. 104, No. 2708 Friday, 22 November 1946

Research and Medical Practice

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AS A STUDENT OF MEDICINE some 30 years ago, I was greatly attracted and stimulated by the prevailing aura of what might be called the romantic period of medical research. The light in Europe had moved about during the previous decades between France, Germany, and contiguous countries. Just then it was strongly emanant from Germany. Its reflections had reached American shores during the preceding quarter of a century, and new luminous centers were arising where the rays touched.

For some time scientific research had made such accelerating strides as to justify completely, in the minds of the intellectually optimistic, the idea of progress of mankind, which at first, with faltering steps, had gathered much strength with the industrial growth of the 19th Century. The theory of evolution was appropriated by Herbert Spencer as a summons to better and nobler ends through knowledge and adaptation. Scientific research was illuminating concepts of biological phenomena and their obvious implications for understanding, preventing, and eventually curing disease and alleviating suffering.

The cell theory had been established by Schleiden, Schwann, and Rudolph Virchow.

The germ theory of disease had, under the subtle tutelage of Pasteur, Koch, and their schools, grown from a lusty youngster to full stature in bacteriology.

Sanitary science and immunology, too, for the well informed, were promising offspring.

Could not all physiological functions and biological phenomena generally be brought to the experimental test?

Lavoisier's chemical interpretation of respiration and Wöhler's synthesis of urea surely left little room for the old concept of a vital activity which would forever be beyond the ken of materialistic searchers.

So it had seemed to Claude Bernard, who had predicted great advances in experimental medicine from a firmer foundation of scientific physiology which he himself had laid with a deft though largely single hand by the aid of chemistry. His predictions were coming true.

The industrial revolution had already realized stupendous material fruits from the trees of mathematics, chemistry, physics, and mechanics. The rich financial and economic rewards were certainly potent catalysts to greater and better things to come. Even the crowding of cities, with increasing density of industrial populations, and the demands of efficiency in production called of themselves for improvement of sanitation and greater protection of health—from an economic, if not from a humanitarian, point of view.

In the meantime, to sustain this rapid growth, financial support had to be forthcoming for the institutions within which the necessary technological training and scientific research were to be pursued. The fulfillment of this demand became increasingly disproportionate to the zeal of the growing, but none too numerous, young scientists and their academic houses.

Wealth from industry in our country accumulated rapidly through the instrumentalities of research and the application of its powers. The public spirit and generosity of philanthropic industrialists, together with limited State and Federal subsidies, gave the necessary stimulus and support for promotion of science in the early part of this century. In other countries government funds, supplemented by industry and private capital, provided the means. Thus reinforced, the idea of progress came marching blithely up the path of the 20th Century, led by the hand of science and nourished more and more with the economic fruits of research. Then progress, in its onward march, seemed to stumble, to stop dead in its tracks. Civilization shook with the convulsion of World War I, involving profoundly the German nation that for a full century had been most zealous for science.

The convulsive seizure was followed by the coma of a great depression. Chills and fevers ensuing were succeeded by the more violent convulsions of World War II, from which our patient even now shakes to his depths, but with intervals sufficiently lucid to perceive that, while his head and heart are bewildered and faint from his travails, his muscles and bones have

Based on an address delivered in Baltimore, Maryland, 15 May 1946, upon receipt of the award of the Passano Foundation, Inc.

grown stupendously strong through the titanic struggle.

During our period of growth, when investigations were increasing in number and in effectiveness, when universities were being provided with greater means for research, these private means played an indispensable role both in creating and in supporting the scientific environment. The needs have now outgrown this resource; furthermore, the time has come when greater responsibility should be delegated to the universities and investigators themselves, and in order to accomplish this the universities must be provided with large sums of money for education, research, and training as free as possible of restrictions.

Some private philanthropic foundations were very liberal in their organization; others were highly circumscribed in their operation; all of them, as matters stand, are severely limited in their financial capacities to meet the growing demands of research. The result is that by design, or necessity, or both, funds now available for medical research are inadequate in amount and usually expendable in the form of short-term grants for specific "projects" determined by the objectives of the donor or administrators. "Projects" tend to be selected for their developmental value rather than because of fundamental significance. The aid provided has been helpful and often essential to bringing initiated research to a useful conclusion, but the price paid is, to a considerable extent, a release by the investigator, the teacher, and the university of the only thing worth while academically—the responsibility for originality and initiative in the free pursuit of intellectual curiosity.

The board of trust of a university or a foundation is not willing, or able, freely to absorb the risk of original research. It prefers to play safe by investing in the development of occasional and fortuitous revelations of widely applicable principles and methods.

The limited tenure of research positions under short-term grants is precarious and injurious for the investigator in training or pursuing a career. The determination and direction of fields of research by the distant control, often from beyond the grave, of available funds is inhibitory and stultifying to those who prefer to follow freely the bent of their own curiosity.

In some instances a foundation has sought to remedy the situation by granting "fluid" research funds to certain medical schools to be administered by the faculty of the school itself. Wherever this has been tried I believe it has been eminently successful.

So, in the rapid development of medical research and teaching in this country, a dual mechanism has evolved: the university, the institution of learning, is largely controlled in its research policies and provisions by extramural influences.

Industry has not devised means of affording a free financial aid to universities; if anything, its aid, with few exceptions, is the most restrictive. It would seem entirely possible for industry to provide much greater aid to university training and research in science, provided industrial resources were pooled and allocated to universities in the form of "fluid" funds for fundamental, basic, or, as it is sometimes called, "pure research."

But postwar trends and developments seem to be fashioning a different procedure for support of scientific research and training—a procedure full of both promise and pitfalls. This procedure involves support, in and out of universities, by means of public or government funds to be administered through a mechanism simulating in important respects the private foundations, represented by the proposed National Science Foundation, but threatening to continue, possibly to a disadvantageous degree, the industrial plan of "project" development inherited from wartime needs and psychology, and including the element of political interest.

Regardless of possible disadvantages in its administrative machinery, one should emphasize that the legislation proposed recognized the importance of the interrelationship and interdependence of the sciences. All knowledge gained through research has a meaning for medicine, and, more specifically, we well know the dependence of medical research upon the natural sciences. Modern movement has related medicine to the university in such a way that medical research and medical practice are becoming more and more dependent upon these institutions of learning, so that whatever affects the university deeply concerns medicine. A place within our social structure such as the university, where serious students might forgather and freely, patiently, dispassionately, and objectively search fact and principle, would seem to be good in itself, even though it should lead to some concepts contrary to current thought. Although there is a near-universal demand and general acceptance of additions to knowledge in medical research, it would be regrettable if the privilege of freedom of thought and research should be justified only on the assumption that basic or "pure" research might lead to the discovery of facts, methods, and general principles that could be exploited usefully by contemporary local or national standards. Unfortunately, the universities have become merely the operating agencies for trustees and administrators of funds who reserve for themselves, in large measure, the privilege and responsibility of determining the trends of research, the training of scientists, and the extent and quality of the result.

My contention is that such privilege and responsibility should properly repose in the university facul-

ties, and could do so were it not for lack of money—an amount of money that would appear almost negligible in the accounting of our national fiscal affairs. One fears the industrial approach with its determination to get a job done as quickly as possible even in a National Science Foundation. The "job" is referred to in current usage as a "project," and the industrial form of management involves a decision, by those responsible for money, as to what projects should be supported and what not.

Following present practice the scientist himself in the university would be permitted as at present only to seek financial aid by submitting plans for his "project." A great deal of his time and energy are now devoted to this necessity to sell himself, his department, his insecure staff, and his university on a restricted market in order to devote the time that is left to scientific inquiry.

The public is satisfied to have the university authorities select teachers to staff their various faculties for the routine instruction of their sons and daughters, but there seems to be something more important about the conduct of research—really the highest form of teaching—something requiring regimentation and control through financial restrictions that to my mind is entirely incompatible with the best interests of research. I hope that this will not be projected into the future.

I believe the crux of the situation lies in the fact that exploratory research—teaching research, if you will—research that seeks basic principles, inapplicable until thoroughly understood, entails relatively great financial waste. The university does not have the financial resources to absorb the waste or rejections in its budgets, and donors of grants-in-aid, often not scientists themselves, try to select "projects," preferably of a developmental type, with as little risk of waste and failure as possible. *But the true interests of science require investigations that involve great risk, and if ultimate progress is to be expected in the application of scientific knowledge to human needs, the cost of the waste of original research must be met.*

It is to be hoped that those who should be responsible for the expenditure of public funds for scientific research and training will concern themselves more with the provision of conditions, in universities at least, that would be congenial and attractive to the investigators and students who need a liberal environment for the pursuit of problems to which their intuition and curiosity lead them, and whose satisfaction lies primarily in understanding rather than in utility. It is impossible to do this by contract or by a grant-in-aid of a "project." In addition to the grant-in-aid type of support, money in large quantity must be given to the universities to be spent by faculties at their own discretion for promoting research and absorbing its risks, as they may determine, to suit their own needs.

It is my opinion that, should money for research be provided by the Government, the philanthropic foundations should consider ways and means for providing from their funds the basic requirements of teaching faculties in order that teaching and training might continue on a level commensurate with research opportunities. To supplement the educational needs of science, these faculties, once secured, should be provided liberally with grants from government appropriations of the "fluid" type which would be expendable at the discretion of the faculties themselves to meet the needs of exploratory or basic research as a part of the teaching and training function. Grants-in-aid for developmental research should be provided also, but when a "project" is brought up to this level, there is relatively little risk involved and it is easier to judge of potential fruitfulness.

The great threat of our age to human welfare, as I see it, is that societies led or driven by industrialism are gathering the individual into their fold as a service unit. The individual as a member of society thus must do a society's bidding, regardless of the particular pattern that social organization might temporarily represent. To the true scientist, the present frame of social organization is not the end of all wisdom but just another phenomenon to be viewed objectively in the course of his inquiries. The scientist's limits are the boundaries of the universe, and his function cannot, without destroying him, be limited to the service of any particular social order. Industrial, social, religious, and political patterns are not yet drawn to serve mankind. It is to be hoped that each governmental power will provide an oasis for students who are individual elements of mankind first and servants of society last. Otherwise, intellectual growth will wither and die. Medicine is dedicated to the service of man and not to a social order. In this relation, medical research in its broadest sense has a pre-eminent call upon every social structure for support not merely for immediate needs but for the discovery of broad principles upon which the health of mankind depends. Let each social order therefore give the scientist a free hand and provide him with the environment and the tools he needs; make him accessible to students, for he is essentially a teacher; make the university his home; and otherwise, for humanity's sake, leave him alone.

Legislation to be considered in the next session of Congress is sufficient evidence of a changing social order, should we need more evidence than we have seen in past sessions. Proposed legislation would aid medical science by providing money for the train-

ing of scientists and facilitating their work of inquiry; other proposed enactments would affect the structure of medical practice. The latter disturbs organized medicine, for it is fearful of change and reorganization upon a different pattern. Awakened from its lethargy of conservatism, organized medicine has bestirred itself in an attempt to meet the challenge and still preserve its values, and there are values I believe worthy of preservation in so far as a physician is a servant of humanity. In those areas of conflict of interest where the best attainable medical practice is opposed by considerations of the best possible financial return to the doctors, there is little doubt that society will make the proper choice.

The practitioner of medicine, however lofty his ideals, has hardly realized the changes in his environment which medical science and social reorientation have brought about in this industrial age. The limitless authority he once possessed as the exponent of all theory and practice, as he called it, has rapidly been pared until in considerable measure he has become a relatively insecure specialist.

The first great inroad upon the domain of medical practice came by way of public health, or what physicians used to call state medicine. The real public health movement was founded upon the discoveries of the last half of the preceding century in the field of bacteriology. With the discovery of the etiological agents of many infectious diseases and their mode of spread, it became possible to institute preventive measures, such as water purification, sanitation, and food protection. Immunizing procedures were likewise devised that can be cared for by the health services. More recent research, particularly concerning the vitamins, has made it possible to remove the nutritional diseases and impairments as individual problems of the practicing physician to the sphere of public responsibility. Industrial hazards likewise are no longer in general the responsibility of the private practitioner. Increasing knowledge of chemistry, physics, physiology, pathology, and bacteriology have further limited the physician's authority, for now he must resort to expert advice from the laboratory for the fundamental knowledge necessary for diagnosis, prognosis, and even treatment. Electrocardiography, X-ray, chemical, bacteriological, and serological tests, the microscopic examination of tissues and specimens, have become such technical procedures and are so necessary to modern medicine that the practitioner cannot do without them and must rely upon the reports of specialists in these subjects.

There are also less exact but broader areas in which the physician has lost prestige, authority, and influence, namely, the social aspects of disease. The physician is being taken from the home of the sick to the hospital ward. When formerly he knew the hereditary, family, home, personal, and economic environments of his patients, he was presumably better qualified to judge of their importance in disease than he is today with office and hospital practice demanding such a large proportion of his time and energy. Consequently, social agencies are taking over where he has left off—the social service departments, the social worker, the nurse, the public health services are all concerned now with the environmental factors and the social implications of health. Especially is this true in our industrial environments. Research and the public conscience are two important factors in the rapid disintegration and redistribution of the competence and authority of the old family doctor of less than a century ago. Research has played the predominant role and has necessitated the creation of specialties.

In the hospital and the medical school there should eventually come to a focus the mutual interdependence of the various facets in the kaleidoscopic picture of modern medicine, and all in turn will find their most congenial and productive setting and their culmination in the university. The greater and greater dependence of medical research upon the natural sciences and the increasing need for cooperative relationships of the social sciences with the humanities will lend new and greater meaning to the university in terms of its public relations, responsibilities, and services. A tremendous opportunity lies before the public to elevate the university to the sphere of influence and effective humanitarian activity that it is designed for, through adequate support, spiritual and financial, for these institutions of learning.

The Passano Foundation Award, which Dr. Goodpasture won in 1946, is an unusual one **because it comes not from invested capital but from the operations of the Williams and Wilkins Company, Medical Publishers of Baltimore, of which Mr. Passano was president. The award, established for the purpose of advancing medical research, was granted for the first time this year, a few weeks before Mr. Passano died. Plans have now been made to continue the award as a memorial to him.**

Dr. Goodpasture received the award for his original development of the method for propagation of viruses in pure culture by inoculation of chick embryos and for his outstanding contributions to advancement of knowledge of the cell-parasite relationship in bacterial and virus infection.

The Science Training Group in the Washington Area

Philip N. Powers,[1] ***Executive Secretary***
Washington, D.C.

LOCAL EDUCATIONAL INSTITUTIONS have set up fully-accredited, off-campus graduate science courses for the convenience of government scientists in the Washington area. More than 700 physicists, engineers, chemists, and mathematicians have enrolled in one or more of 26 such courses, usually offered immediately after working hours in a room close to their place of work.

This citywide educational program was initiated by the Civil Service Commission's Advisory Committee on Scientific Personnel, already described on these pages (1946, **103**, 437), as part of its program "to improve the employment status of Civil Service scientists." The shortage of scientific personnel and the unwillingness of many of our best scientists to accept or to continue government employment have placed a serious handicap on the Government's entire science program.

The only way to relieve the shortage is to train more scientists. But to make government service more attractive to scientists, fundamental changes in the employment status of Civil Service scientists are needed. One of the most important of these is to provide *more opportunities for professional growth and development*. This will not only serve to attract and retain high-grade people, but it will improve the competence of those scientists presently employed and therefore increase the value of their service.

Professional advancement of scientists may be encouraged in various ways. One of the most important, however, is to facilitate attendance in the graduate science courses of leading universities. Government scientists usually find this impossible because the courses are given at an inconvenient time, or at too great a distance, or both. Experience has shown, during the months since the end of the war, that this single factor has led many of our ablest scientists to leave government employ and to accept employment where their graduate study may be begun or resumed, as the case may be.

It was for these reasons, as well as to help alleviate the shortage of scientific personnel, that the Advisory Committee created the Science Training Group in the Washington area to do a job similar to that suggested by the writer in an earlier issue (1945, **101**, 612). The assigned purpose of the STG is: "To evolve, subject to the approval of the Advisory Committee on Scientific Personnel, a program for facilitating and encouraging the further training of scientific personnel, initially at the graduate level, and to carry out this program."

The STG came into existence early in 1946, with representatives from the Departments of Agriculture, Commerce, Interior, Navy, and War, and the Federal Security Agency. Dr. Marsh W. White, professor of physics at the Pennsylvania State College and expert consultant to the War Department, was chosen chairman. The activities of the Group since then have been primarily to determine (1) the particular graduate courses most needed by government scientists in the Washington area, and (2) the best procedure for establishing these courses (if not already conveniently available) so as to ensure high quality and so that they will be acceptable for meeting graduate degree requirements.

Determination of the courses needed. Merely to pass a questionnaire around to the 10,000 scientists in the Washington area, asking them to indicate the courses they would like to take, is not an accurate means of determining the need. (This was done, however, in a preliminary fashion in the short time that was available to discover the most urgently needed courses prior to the beginning of the spring semester.) There are two reasons why the method is inadequate. First, a potential student needs a list of courses from which he may choose, and second, he needs the advice and counsel of a man experienced in working with graduate students.

For these reasons the STG adopted the following procedure:

(1) Each participating agency was advised to establish its own "Advisory Committee on Scientific Education and Training" for the purposes of (a) making intelligent guesses on the courses which ought to be available to its personnel, and (b) encouraging its personnel to obtain competent advice and counsel in planning educational programs.

(2) Each of these agency committees was asked to submit its suggested course list to the STG.

(3) All of these submitted course lists were then combined into one and circulated to scientists throughout the Washington area with a questionnaire and a note describing the procedure, and suggesting that a long-range program be planned as part of the process of filling out the questionnaire.

(4) The data were then analyzed to show not only what courses were needed but also *where* they were needed.

As a consequence, the STG now has a far more accurate picture of the graduate training needs in

[1] Science Education Adviser of the Scientific Personnel Branch, Office of Naval Research, Navy Department. Because of the large number of Navy scientists in the Washington area, the Navy was able to provide the necessary facilities to carry out much of the actual operation of the program of the Science Training Group.

science in this area than has heretofore been available. The picture is expected to be continuously improved in accuracy through additional surveys, follow-ups on questionnaires received, further consultation with those now registered, and the activities of the various agency committees.

Establishment of the needed courses. Transportation difficulties usually require that the courses be set up on the premises of the particular agency where a majority of those needing a given course are employed. It is not customary, however, and in some cases not feasible, for universities to establish fully-accredited graduate science courses off the campus. The necessary controls to assure high quality become more precarious, and the additional burden on universities already overwhelmed with students is almost unbearable. Nevertheless, it was believed essential by the STG that these difficulties be overcome. The cooperation of local educational institutions, in particular the University of Maryland and the U. S. Department of Agriculture Graduate School, is making it possible to establish many of the needed courses.

To assist the educational institutions in carrying this additional burden, the STG established within itself a "Standards Committee" composed of members familiar with graduate study problems. This Committee

(1) Reviews the data to ascertain the genuineness of the need for a given course in a given agency, in order not to bother an educational institution with a request for a course which will not be supported by a sufficient number of qualified students.

(2) Locates potential instructors, reviews their qualifications, and, if acceptable, recommends them for consideration by the particular educational institution involved as a possible addition to its staff. (This is, of course, unnecessary, if the institution is already adequately staffed to handle the course.)

(3) Assists the institution in ensuring that those who register in a given course have the proper prerequisites.

(4) Reviews the proposed course in all other matters pertaining to its quality. It is intended that the courses established through the STG requests shall be unexcelled.

(5) Evaluates the quality of each course as it is taught.

In order that there shall be complete understanding in matters of policy and procedure, an informal agreement has been reached between the Standards Committee and the cooperating institutions. This agreement makes clear the over-all purposes of the program as well as the registration procedures, the role of the Standards Committee, and the full accrediting of all the STG-requested courses.

Of the 26 courses being established this fall in the fields of physics, mathematics, chemistry, and electrical, mechanical, and aeronautical engineering, the largest group (10) is being established at the Naval Research Laboratory, which, along with the Naval Ordnance Laboratory and the David Taylor Model Basin, had initiated programs of their own before the organization of the STG.

As an additional service to Washington scientists planning graduate study programs, the STG prepared and distributed 6,000 copies of a list of *all* graduate science courses being offered in the area this fall. The list gives the course numbers, titles, credits, times and places, and the instructor, along with pertinent information about registration and sources of additional, more detailed information. The graduate offerings in science of the U. S. Department of Agriculture Graduate School, the Catholic University of America, Georgetown University, George Washington University, Howard University, the University of Maryland, and the National Bureau of Standards Graduate School are listed.

This program of the STG, now in its initial stages, is frankly directed toward cooperating with the local educational institutions so as to make Washington a center in graduate science education which is commensurate with its role as a center of scientific research.

There are other areas into which the STG may expand its activities if so directed by the Advisory Committee on Scientific Personnel. These include (1) the encouragement of similar programs outside of the Washington area, (2) the development of a similar program at the undergraduate level, and (3) the organization of cooperative "in-service" training programs for scientific personnel. All three of these areas are already developing independently of the STG. Cooperative programs between universities and government agencies are under way and in a few cases are of long standing in several parts of the country. The undergraduate area is being explored by the Naval Research Laboratory and the Bureau of Ships, Navy Department. The Department of Commerce, in cooperation with several other departments, has recently conducted an in-service training program on wartime developments in electronics.

Although these training programs operate on only a portion of the problem, they should nevertheless go far toward improving the attractiveness of Civil Service employment for high-caliber scientific personnel. The extent to which these scientists can be both attracted and retained will determine the extent to which the Government will actually accomplish the tremendous scientific tasks which the people of the United States have declared through Congress should be done.

Technical Papers

The Infectiousness of Coccidioidomycosis

SOL ROY ROSENTHAL, MAJ., M.C., and
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Coccidioidomycosis is an infectious disease caused by the fungus, *Coccidioides immitis*. The respiratory tract is the usual portal of entry. The fungus causes either a benign, self-limiting disease of the lung or a progressive, chronic and malignant process which may spread from the lung to localize in any or all organs of the body. The disease is endemic in San Joaquin Valley, California, as well as in parts of Texas, Arizona, and New Mexico. With the training of troops in these states, and their subsequent demobilization, numerous soldiers harboring the fungus will return to all parts of the United States.

It is universally reported that the disease is not contagious, there being no direct man-to-man or animal-to-man spread, and that there is therefore no reason for elaborate isolation (*1–4*). The general consensus of opinion is that the spherule or endospore-filled sporangium stage of the fungus found in animal tissue goes through a stage of development in nature to produce mycelial threads and spores (chlamydospores), when it becomes infective by the respiratory route for humans and animals. Rodents have been considered the reservoir for the disease (*1*).

The following experiments demonstrate that it is possible to transmit the disease, by bronchial installation of spherules, from man to animal and from animal to animal. These findings must alter our stand regarding the isolation of diseased patients.

The method employed was to instill spherule-containing exudates into the bronchi of guinea pigs (by means of a catheter or blunt needle) and to propel the exudate into the smaller bronchi ramifications and alveoli by applying a minimal amount of air pressure. This method was used by the senior author to produce lung abscesses in dogs and was later modified by Robertson to produce lobar pneumonia.

Sixteen guinea pigs were thus injected, using exudate from a sacroiliac abscess, a psoas abscess, and an emulsion of hilus lymph nodes from a human case and from a neck abscess of a guinea pig. The animals (14) were sacrificed at various intervals from 8 to 63 days (two died at 18 and 28 days). Infection localized to the lung occurred in every case varying from a typical primary complex of the lung, where a single lesion was noted in one lobe, and a corresponding enlarged hilus lymph node, to the involvement of all lobes simulating lobar pneumonia. Generalization did not occur in any case.

Microscopically, typical granulomata containing spherules in every stage of development were noted in the lung and draining lymph nodes. Direct NaOH mounts and/or cultures of lungs and nodes were positive for *C. immitis* in practically every instance.

The gross and microscopic lesions (especially the single localized lesions in the lung) more closely resemble the human infections than those produced in animals by the inhalation of chlamydospores.

These experiments show that the spherules direct from human or animal sources are infective through the respiratory tract. Thus, all active human cases of primary or secondary coccidioidomycosis should be considered contagious until proven otherwise.

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Effect of Rubber Tubing Upon the Stability of Penicillin and Streptomycin Solutions

J. B. HUELSEBUSCH, M. J. FOTER, and I. W. GIBBY[1]
Department of Bacteriology, Research Laboratories
The Wm. S. Merrell Company, Cincinnati, Ohio

S. L. Cowan (*1*) has reported the inactivating effect of synthetic rubber upon solutions of penicillin. Since no work upon this important problem has been reported in the United States, we have investigated the suitability of a variety of rubbers for the parenteral administration of penicillin and streptomycin.

Solutions of penicillin and of streptomycin were placed in separate sterile three-foot lengths of the various samples of rubber tubing. For controls, the solutions were also placed in glass tubing. At the end of 6 and 24 hours samples were withdrawn for assay.

The solutions of streptomycin were assayed by the filter-paper disc method with *Bacillus subtilis* as the test organism. The penicillin solutions were assayed according to directions given in "A tentative penicil-

[1] We wish to express our gratitude to the B. F. Goodrich Company, Harshaw Chemical Company, Fisher Scientific Company, and Chemical Rubber Company for samples of rubber used in this investigation.

lin-sodium monograph" (Washington Conference, 17 February 1944).

The effects of the various rubber samples upon the stability of penicillin and streptomycin solutions are shown in Tables 1 and 2, respectively.

TABLE 1

EFFECT OF SYNTHETIC AND NATURAL RUBBERS UPON THE STABILITY OF PENICILLIN SOLUTIONS*

Description	Type	Unitage at end of 6 hr.	Unitage at end of 24 hr.
White surgical Koroseal	Synthetic	70	36
GN black	"	95	16
Black Koroseal	"	97	73
S black	"	111	86
Buna	"	82	0
Buna white	"	121	114
White plastic	"	111	93
Neoprene black	"	74	0
Pure gum black	Natural	96	0
GRS black	Synthetic	79	0
Buna S	"	50	0
Tygon	"	91	85
Amber latex	Natural	87	94
Crepe rubber	"	105	99
Natural rubber	"	117	93
Anode amber	"	105	93
Glass tubing	.....	108	106

* The solution was made up to contain 100 units/ml.

TABLE 2

EFFECT OF SYNTHETIC AND NATURAL RUBBERS UPON THE STABILITY OF STREPTOMYCIN SOLUTIONS*

Description	Type	μg./ml. at end of 6 hr.	μg./ml. at end of 24 hr.
White surgical Koroseal	Synthetic	37	43
GN black	"	40	49
Black Koroseal	"	40	50
S black	"	40	39
Buna	"	43	50
Buna white	"	46	39
White plastic	"	43	40
Neoprene black	"	43	34
Pure gum black	Natural	40	44
GRS black	Synthetic	34	44
Buna S	"	46	43
Tygon	"	43	50
Amber latex	Natural	46	34
Crepe rubber	"	43	34
Natural rubber	"	40	56
Anode amber	"	40	54
Glass tubing	.....	34	42

* The solution was made up to contain 50 μg./ml.

Of 11 samples of synthetic rubber tested, 4 inactivated penicillin completely in 24 hours. Two other samples caused 64 and 84 per cent reductions in the activity of the penicillin during the same period. Of 5 samples of natural rubber tested, 1 pigmented sample inactivated penicillin completely in 24 hours.

Buna S rubber caused a 50 per cent reduction of penicillin activity in 6 hours. Other samples of synthetic rubber reduced the activity of penicillin 20–30 per cent in the same period.

None of the samples of rubber tubing tested caused any reduction in the activity of streptomycin.

This study is not intended as a complete investigation of the effects of rubber upon antibiotics. It is evident, however, that for continuous drip procedures some attention must be given to the type of rubber used for the administration of penicillin. It is of interest to note that white surgical Koroseal caused a drastic reduction in penicillin activity, while black synthetic Koroseal caused only a moderate inactivation of the antibiotic.

It is suggested that rubber tubing intended for hospital usage be checked for inactivating effects upon antibiotics and that acceptable tubing be appropriately designated.

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Comparative Toxicity of DDT and Four Analogues to Goldfish, Gambusia, and Culex Larvae

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The large-scale use of DDT in natural areas makes it necessary to study the effects it and related compounds have on all forms of life if control measures are to be developed.

Of beneficial vertebrate groups, fish have already been shown to be very vulnerable to DDT in the laboratory (*2, 3*). Under natural conditions mortality of fish has been observed where large amounts or repeated doses of DDT were used in the control of mosquito larvae (*7*). We have attempted to determine more accurately the comparative tolerance of fish (goldfish and *Gambusia affinis*) and mosquitoes (*Culex apicalis*) to DDT and especially its p-halogen analogues.

Procedures. In addition to the regular DDT or 1-trichloro-2,2-bis(p-chlorophenyl)-ethane (*1*), four analogues were also tested as follows: (1) 1-trichloro-2,2-bis(phenyl)-ethane, which we shall designate as DPT; (2) 1-trichloro-2,2-bis(p-fluorophenyl)-ethane DFDT; (3) 1-trichloro-2,2-bis(p-bromophenyl)-ethane DBrDT; and (4) 1-trichloro-2,2-bis(p-iodophenyl)-ethane, DIDT.[1] Summerford synthesized these compounds by condensing benzene or the appropriate halobenzene and chloral with the aid of chlorosulfonic acid, according to a previously described method (*6*).

All tests were run in individual fish bowls containing tap water previously conditioned and oxygenated in a large aquarium containing aquatic plants. One fish and 4 to 10 Culex larvae were placed in each bowl. One ml. of an acetone solution of DDT and its analogues, ranging from 0.0005 to 10 ppm, was added to

[1] The preparation of the p-fluoro and the p-iodo analogues will be described in a subsequent paper, since we have found no published reference to the synthesis of the former compound.

each liter of water. Controls containing 1 ml. of pure acetone in 1 liter of water had no detectable effect on the test animals. A three-day period was selected as a somewhat arbitrary time limit for the experiments, and experiments were repeated two or three times at critical concentrations.

Results. The results of the experiments are shown in Fig. 1, which indicates at a glance the comparative tolerance of the organisms to the various compounds. The solid bars indicate the range of concentrations

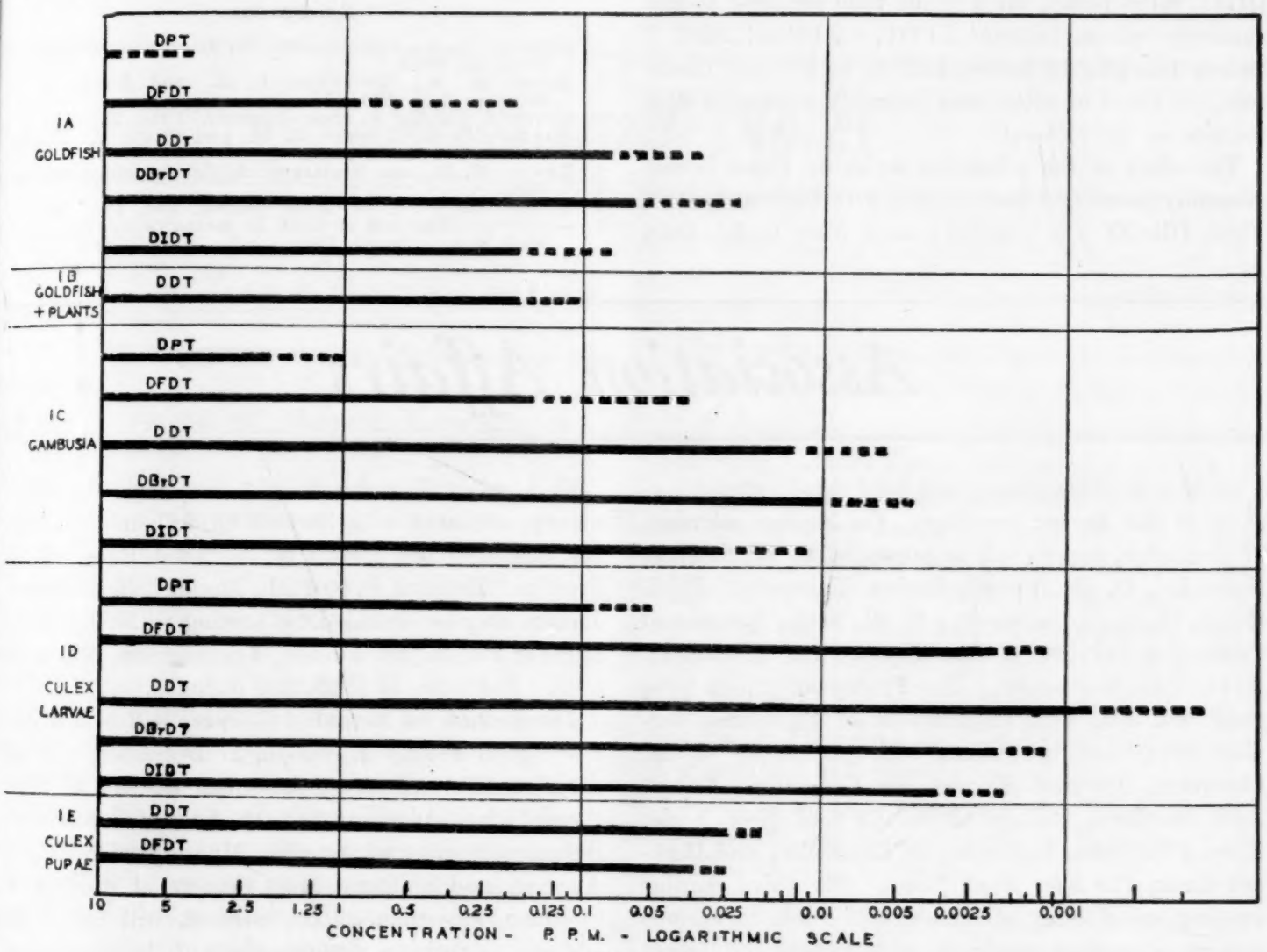

FIG. 1

producing 100 per cent mortality of fish and 95 per cent or greater mortality of mosquito larvae; the broken part of the bars indicates concentration producing partial mortality. It should be emphasized that the resistance of individuals is so variable at lower concentrations that the setting of the lower lethal limits must be somewhat arbitrary. Gambusia proved to be much less resistant than goldfish under these conditions. As far as DDT itself is concerned, the median lethal dose is approximately 0.1 ppm for goldfish, 0.01 ppm for gambusia, and 0.001 ppm for larvae. Therefore, the goldfish were 1/100 and the gambusia were 1/10 as susceptible as the mosquito larvae, provided the DDT was evenly distributed in the water and therefore had equal chances of penetrating the organisms. Mosquito pupae were much more resistant than both the larvae and gambusia. Not only did they survive relatively high concentrations of DDT and DFDT for three days, but many subsequently emerged into normal adults.

As shown in 1B (compare with third bar, 1A), the presence of aquatic plants in the bowls (10 grams wet weight of *Elodea* and *Cabomba*) reduced the toxicity considerably as far as fish were concerned. The plants themselves were unaffected. Some bowls containing high concentrations of DDT developed thriving colonies of common algae, *Scendesmus*. As previously reported (*5*), DDT appears not to be a direct cell poison.

The unsubstituted compound, DPT, was found to be comparatively nontoxic. DFDT was moderately toxic to fish, while DDT and DBrDT were very similar, being about 10 times more toxic to fish. DIDT proved to be somewhat less toxic than DDT. It should be pointed out, however, that since DBrDT and DIDT have a greater molecular weight than the chlorine analogue (DDT) there are actually fewer molecules of the former at any given concentration by weight.

Therefore, molecule for molecule, the DIDT would have to be rated more toxic than DDT; and DBrDT would be the most toxic of all as far as these fish were concerned. Very roughly speaking, the toxicity of this series tends to increase with the weight of the molecule.

Perhaps an even more interesting difference in the series is in regard to speed of action. When concentrations of comparative toxicity were prepared (DFDT, 1 ppm; DDT, 0.1 ppm; DBrDT, 0.1 ppm; DIDT, 0.166 ppm), the average time required to kill gambusia was as follows: DFDT, 4.5 hours; DDT, 7 hours; DBrDT, 16 hours; DIDT, 54 hours. Therefore, the speed of action was inversely correlated with the size of the molecule.

The effect of the p-halogen series on Culex larvae generally paralleled that on fish, with two exceptions. First, DBrDT was relatively more toxic to fish than to mosquito larvae as compared with DDT. Hansen, *et al.* (*4*) found DBrDT to be similar to DDT but less toxic to land insects. Second, DFDT was relatively more toxic to the larvae than to fish (Fig. 1). For this reason, DFDT may have possibilities as a larvicide; at least it seems worthy of field tests, especially in view of its rapid action.

Determinations of the residual toxicity of the analogue series are now being made, and the results will be reported in a subsequent paper.

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Association Affairs

Section Q (*Education*) will hold three regular sessions at the Boston meetings. On Friday morning, 27 December, papers will be presented by W. E. Hall, Nebraska; D. D. Durrell, Boston University; P. J. Rulon, Harvard University; C. W. Scott, Vocational Counseling Services of New Haven; and Francis H. Horn, Yale University. The Friday afternoon program will deal with implications of the armed services educational programs, with papers by M. M. Chambers, American Council on Education; Robert John Matthew, College of the City of New York; Elwood C. Davis, University of Louisville; and Howard Rusk, *The New York Times*. The third regular meeting, on Monday afternoon, will relate to various aspects of science teaching, with papers by Robert Stollberg, Wabash College; Paul Blackwood, The Ohio State University; Robert Wickware, Willimantic State Teachers College; Hubert Evans, Teachers College, Columbia University; and Benjamin C. Gruenberg, New York. Sections Q and I will have a joint session on Saturday evening, at which the vice-presidential addresses of the two sections will be given. Section Q is also cosponsoring several other special programs, including a symposium on scientific personnel, Saturday morning and afternoon, with Sections K, I, and B; a symposium on the teaching of ecology, Saturday afternoon, with the National Association of Biology Teachers; and a joint session with Section L, Monday morning, on "The Place of the History of Science."

Pi Lambda Theta, women's honorary educational society, affiliated with Section Q, will hold a dinner for members and guests in the Oval Room of the Bradford Hotel at 6:00 P.M., Monday, 30 December. Tickets may be obtained by writing to Mrs. Dorothy Larned, 154 Maynard Road, Framingham, Massachusetts. The price is $3.25, tax included.

The Section on Botanical Sciences will hold a joint meeting on Friday afternoon, 27 December, with the American Fern Society, American Society of Plant Physiologists, American Society of Plant Taxonomists, Botanical Society of America, Mycological Society of America, and Sullivant Moss Society, at which E. C. Stakman, chairman of the Section, will deliver his address, as retiring vice-president of the Association, on "The Nature and Importance of Physiologic Specialization in Phytopathogenic Fungi." This will be followed by a symposium on plans for union involving workers in the biological sciences. Paul J. Kramer, H. B. Tukey, Ralph E. Cleland, and R. F. Griggs will speak briefly on various aspects of the proposals, after which the meeting will be opened for questions and discussion.

The Society for Research in Child Development will hold meetings on 27–28 December. In addition to a business meeting on Friday, 27 December, there will be two symposia; "Methodological Problems Met in Integrating and Interpreting Physical, Medical, Psychological, and Social Data in Longitudinal Studies of Children," with Wayne Dennis presiding; and "Psy-

chological Problems Met in General Medical Practice With Children," with Arthur T. Jersild presiding. The Saturday morning session, 28 December, with Kurt Lewin presiding, will include nine research reports. Saturday afternoon will be devoted to the topic: "The Effects of Severe War Conditions Upon Child Development and Behavior," with Harold C. Stuart presiding. Frank Gollan will discuss "Child Health and Development and War." Dr. Gollan was scientific director of the Nutrition Mission to Italy sent out by the Unitarian Service Committee to make sample surveys of nutritional and epidemiological conditions throughout Italy and report to UNRRA.

Section I (*Psychology*) will meet on Saturday and Sunday, 28–29 December. Seventeen papers will be presented. Saturday morning and Sunday afternoon will be devoted to general psychology and Saturday afternoon to clinical psychology. Saturday evening the Section will meet jointly with Section Q to hear the addresses of the vice-presidents of both sections.

News and Notes

About People

The 1946 Nobel Prizes in physics and chemistry have been awarded to four American scientists, according to an announcement from Stockholm on 14 November.

P. W. Bridgman, of Harvard University, was selected for the physics award for his production of extremely high pressures and his discoveries of resulting effects of the pressures.

J. B. Sumner, of Cornell University, who isolated the first enzyme in 1926, received one half of the chemistry award for his distinguished research in the field of enzymology. The second half was awarded jointly to John H. Northrop and W. M. Stanley, of the Rockefeller Institute, Princeton, for their preparation of virus proteins in pure form.

Dr. Stanley was the recipient of the 1936 AAAS $1,000 Prize for his paper, "Some biochemical investigations on crystalline tobacco mosaic virus proteins."

As previously reported in *Science* (8 November, p. 440), H. J. Muller, of Indiana University was awarded the Nobel Prize in medicine and physiology on 31 October. Dr. Muller's work had been recognized by AAAS in 1927 whe he was cited for his paper "The influence of X-ray on genes and chromosomes."

H. K. Skramstad has been made chief of the Guided Missiles Section, National Bureau of Standards. This Section is concerned with the extended research and development of the advanced forms of guided missiles. The first fully automatic guided missile to be successfully used in combat by any nation was developed by the Section in close cooperation with OSRD, Massachusetts Institute of Technology, and the Navy Department. This missile is the recently declassified and much publicized BAT. Dr. Skramstad first went to the Bureau in 1935 as a physicist in the Aerodynamics Section. Until the outbreak of the war he was engaged in studies of wind-tunnel turbulence and the investigation of the stability of laminar flow, important in the mechanics of air flow over surfaces. In 1942, he became technical assistant in the development of guided missiles, playing a key part in the development of the BAT.

Robert E. Johnson became the technical director of the Army Medical Nutrition Laboratory at Chicago on 1 October, replacing George H. Berryman. Dr. Johnson has been associated with the Harvard University Fatigue Laboratory since 1935. Dr. Berryman was commanding officer and director of the Nutrition Laboratory from its activation in 1941 until he left to attend the University of Illinois Medical School.

Gordon A. Johnsgard has been named professor of soil science and soil scientist to the Experiment Station at the North Dakota Agricultural College, Fargo. Dr. Johnsgard was formerly with the Tennessee Valley Authority as agriculturist.

Nathaniel Coburn, formerly at the University of Texas, has been appointed assistant professor of mathematics at the University of Michigan. Dr. Coburn was a physicist at Laredo Army Airfield during the war.

Visitors From Abroad

Harald Cramér of the University of Stockholm will deliver a series of three lectures on "Some Aspects of the Theory and Applications of Random Movements," 4–6 December, under the auspices of the Institute of Statistics of the University of North Carolina at Chapel Hill. Random movements, or stochastic processes, and their applications in physics, biology and economics form one of the fields of particular concern of the new Department of Mathematical Statistics of the Institute. M. S. Bartlett of Cambridge University

is now conducting work in this field as Visiting Professor of Mathematical Statistics at Chapel Hill.

Alexander A. Mikhailov, of Moscow University, president of the Astronomical Council of the Academy of Sciences of the USSR, will speak (in English) on "How the Soviet Scientists Works," under the auspices of The American Russian Institute, at a luncheon on Saturday, 30 November, at 12:30 P.M., in the Grand Ballroom of the Henry Hudson Hotel, 353 West 57th Street, New York City. Irving Langmuir will be chairman of the luncheon and the discussion. Although admission is by card only, arrangements for attendance may be made through Renier Wyers, Public Relations Director, The American Russian Institute, 58 Park Avenue, New York 16.

Nellie P. Watts, formerly assistant professor of pharmacology at the Women's Medical College, Philadelphia, and later research associate in the Department of Experimental Medicine, New York University, has joined the Pharmacologic Department of Abbott Laboratories, North Chicago, Illinois, as research pharmacologist.

W. H. Hodge, during the past year visiting professor and head of the Department of Botany, Agricultural College of the Universidad Nacional of Colombia, Medellin, has been appointed associate professor of botany at Massachusetts State College. During the war Dr. Hodge served as cinchona botanist with the Office of Economic Warfare and had charge of field exploration in Peru.

Announcements

The Berman Memorial Laboratory, in which many of his former associates and students may carry on his research findings, was dedicated on 1 November to Dr. Harry Berman, a former curator of Harvard's Mineralogical Museum, who was killed late in 1944 while on a war mission. Funds for the laboratory came from fellow workers, former students, and friends of the late scientist, who gave individual contributions. Dr. Berman was born in Boston and was graduated from Harvard in 1931. He studied in graduate courses at Heidelberg, Göttingen, and Cambridge before receiving the A.M. degree in 1935 and the Ph.D. degree in 1936 from Harvard. In 1934 he became assistant curator of the Mineralogical Museum and in 1940 curator and associate professor of mineralogy. In 1944, while on a war mission in the British Isles, the transatlantic plane in which he was flying crashed over Prestwick, Scotland, killing 26 of the occupants.

A new Department of Range and Forest Management has been established in the Agricultural and Mechanical College of Texas at College Station. Vernon A. Young, formerly chairman of the Department of Range Management, University of Idaho, is the head of the new Department. Omer E. Sperry, formerly head of the Department of Biology, Sul Ross College, Alpine, Texas, is in charge of range plants and plant and range ecology. Robert R. Rhodes, formerly of the Soil Conservation Service, Kentwood, Louisiana, is in charge of the forestry work.

Teaching and research in physiological chemistry in the University of Minnesota Medical School has recently been organized as a separate department. Work in this field was formerly administered as a division of the Department of Physiology. Wallace D. Armstrong has been named head of the new Department. New appointments to the Department include: David Glick, associate professor; Elizabeth Frame and Saul Cohen, assistant professors. Others in the Department are: C. P. Barnum, Karl Sollner, and Walter O. Lundberg, associate professors; and Charles Carr, instructor.

The Department of Physics, Illinois Institute of Technology, announces the following appointments: W. E. Bennett, formerly of Rice Institute, Houston, Texas, associate professor in charge of the Van de Graff Laboratory, and R. G. Nuckolls, formerly of the University of Minnesota, assistant professor.

The University of Strasbourg is rebuilding its libraries which were plundered during the war, according to word received by Henry W. Lohse, of Toronto, from M. Tuot, maître de conférences a l'Université, Ecole Nationale Superieur du Petrole et des Combustibles Liquides, 2 rue Boussingault, Strasbourg, France. It would welcome the sending of reprints and other literature published on this continent during the past few years.

Meetings

The 11th International Congress of Pure and Applied Chemistry will meet in London, under the presidency of Lord Leverhulme, on 16–24 July 1947. It is hoped that delegates from many countries will be present. At the 10th International Congress held in Rome in May 1938, it was unanimously decided that the 11th Congress should be held in London in 1941 concurrently with the celebration of the centenary of the foundation of the Chemical Society of London. By reason of the war, both the Centenary Celebration and the 11th Congress were postponed; it has now been decided that both events should take place in London in July 1947. Further information may be obtained from the Hon. Organizer at the following address: The 11th International Congress of Pure and

Applied Chemistry, 56, Victoria Street, London, S. W. 1.

The Midwest Power Conference will be held on 31 March and 1–2 April 1947, with headquarters in the Palmer House, Chicago. Stanton E. Winston, director of the Evening Division at Illinois Institute of Technology, will serve as conference director for the eighth consecutive year. Illinois Tech will again sponsor the meeting in cooperation with nine midwestern colleges and universities and seven engineering societies. The 1946 Conference attracted an attendance of approximately 2,500 persons to hear more than 70 speakers from throughout the United States discuss recent and important developments in the field of power.

Elections

John C. Bailar, Jr., University of Illinois, has been elected chairman of the Division of Chemical Education of the American Chemical Society, succeeding Lawrence L. Quill, Michigan State College. Other officers of the Division are: Edward L. Haenisch, Villanova College, vice-chairman; C. E. White, University of Maryland, treasurer; and Paul H. Fall, president of Hiram College, re-elected secretary.

The Paleontological Research Institution, at its annual meeting, held on 12 October, at its headquarters in Ithaca, New York, elected the following officers for the coming year: Ralph A. Liddle, president; Axel A. Olsson, vice-president; Rebecca S. Harris, secretary; Gilbert D. Harris, treasurer; and Katherine V. W. Palmer, assistant treasurer.

The Connecticut Academy of Arts and Sciences elected the following officers on 24 October: G. Evelyn Hutchinson, president; Alfred R. Bellinger, Frederick A. Pottle, and Herbert Thomas, vice-presidents; Dorothea Rudnick, secretary; Laurence G. Tighe, treasurer; and James T. Babb, librarian.

The American Dental Association installed Sterling V. Mead, Washington, D. C., as president, at its 87th annual convention, held this year in Miami. H. B. Washburn, St. Paul, Minnesota, was named president-elect to take office in 1947. Delegates voted to hold a full scientific meeting in August 1947 in Boston, at the same time the Federation Dentaire Internationale will hold its first meeting. More than 15,000 delegates are expected to attend at that time.

NRC News

The Highway Research Board of NRC will hold its 26th annual meeting at 2101 Constitution Avenue from 5–8 December. The complete program is not yet available but *Highway Research Abstracts* will publish a résumé of the meeting. The publication is available from Roy W. Crumb, director, Highway Research Board.

Fellowships in the Natural Sciences, including mathematics, astronomy, physics, chemistry, geology, paleontology, physical geography, botany, zoology, biochemistry, biophysics, agriculture, forestry, anthropology, and psychology will be available for the year 1947–48. These fellowships are awarded as a rule to persons under 35 years of age who are citizens of the United States or Canada, and who have met all of the requirements for the Ph.D. degree. Applications must be filed on or before 31 December 1946, on forms obtainable from: Secretary of the Fellowship Board in the Natural Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. A handbook describing the fellowships—stipends, conditions, and tenure—will be furnished upon request.

Recent Deaths

John P. Simmons, 66, professor of chemistry at New York University since 1927, died on 29 October. Dr. Simmons began a year's leave of absence this last summer, and had planned to retire as professor emeritus next year.

Louis C. Drefahl, 64, formerly a chemical research engineer with the Grasselli Chemical Company and later associated with E. I. du Pont de Nemours and Company, died on 29 October.

Harvard University's "Science City"

Plans for a "science city" within Harvard's university city, Cambridge, were announced on 2 November by President James B. Conant. The scientific and technological resources of Harvard will be integrated with new buildings and equipment under a new coordination of scientific staffs. A central Science Center Building, now in the process of blueprint planning, will become the axis of the "science city."

Centralization of teaching, study, and research facilities in various scientific departments, now widely spread, will enable many to operate under one roof. In several instances, existing laboratories will be joined to the new science structures.

In the announcement, Dr. Conant stressed the expectation that through this new liaison of scientists and the sciences, Harvard will play an even greater part as a science school in the technology of tomorrow.

It is hoped that the first section of the Science Center Building may be built in the near future with funds now available. An effort is being made to raise the necessary funds and endowment for the entire structure. According to tentative plans, this struc-

ture will be about 500 feet long and four or five stories high, with a frontage on Oxford Street opposite the Mallinckrodt Chemical Laboratory, outside the Yard. This building eventually will house all of the branches of applied physics, geophysics, geology, mathematics, and undergraduate instruction in astronomy, among other groups.

President Conant said:

Construction of this large new science building will complete a science center embracing most of Harvard's scientific activities outside the area of medicine.

We have already located within a convenient radius a varied and well-equipped group of buildings for the fundamental study of the phenomena of physics, chemistry, and biology and their application to astronomy, the earth sciences, and engineering.

The first section of the new science building will be devoted to laboratories required for the new Department of Engineering Sciences and Applied Physics, which has been organized under the Faculty of Arts and Sciences.

Harvard University's contribution to both pure and applied science is in the process of being made commensurate with challenges of the postwar world. The erection of the Computation Laboratory and the Nuclear Physics Laboratories is a first step in this direction.

The new science building, when completed, can be considered as the focus of the integration of our varied activities in natural science. I trust that funds for the construction and endowment of the entire structure may be forthcoming in the not too distant future from a group of interested donors.

Specifically assigned to the central science structure will be the Department of Engineering Sciences and Applied Physics. Frederick V. Hunt, chairman of this Department, is also chairman of the new building planning committee working with the architects.

Other departments with similar assignment are the Department of Mathematics, now scattered around the University; the undergraduate astronomy center, now occupying an inadequate wooden house on Jarvis Street; and large parts of the Division of Geological Sciences, including its branch of geophysics.

Pierce Hall, home of the Graduate School of Engineering, adjacent to the site on which the Science Center Building will rise, is to be joined to the new structure, as will the Cruft, Jefferson, and Research Laboratory of Physics buildings, already under one roof and now devoted to teaching and research in pure and applied physics. The Computation Laboratory, a new building housing the Automatic Calculator, is located close to the northwestern end of Pierce Hall. This building will be ready for occupancy shortly after 1 January 1947. The calculator has been moved from the basement of Cruft Laboratory to the new structure and is being reassembled.

Two cyclotron buildings, now being constructed under joint U. S. Navy and Harvard auspices off the upper end of Oxford Street beyond the University Museum (which is also an integral part of the science center project), will also house a new 700-ton instrument.

The transfer of various University branches and equipment to the new Science Center Building and to new structures will provide increased space for expansion of scientific research and teaching in existing structures now overcrowded.

In the Laboratory

A Color Reaction Given by Streptomycin

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We have observed that streptomycin gives a color test somewhat similar to the Elson-Morgan test (*1*) for glucosamine. The color reaction does not proceed to a noticeable extent if it is carried out with sodium carbonate as proposed by Elson and Morgan for glucosamine. But in the presence of sodium hydroxide the test becomes positive with as little as 50 units of streptomycin. This can be carried out in the following manner: To 2 cc. of an aqueous solution of streptomycin are added 1 cc. of a 2-per cent solution of acetylacetone in water and 1 cc. of 1 normal sodium hydroxide. The mixture is heated for 10 minutes in a boiling water bath and then cooled. A pink color is developed on addition of 2 cc. of a solution of Ehrlich's aldehyde (*1*). The volume is made up to 10 cc., and the light transmission is measured in a photoelectric colorimeter using a filter #540.

Tests carried out on the split products of streptomycin showed that the amino sugar moiety of the streptomycin molecule (*2*), *i.e.* N-methyl-l-glucosamine, is responsible for the color formation. This methylated amino sugar gives the reaction under the

[1] Present address: Department of Pharmacology, College of Physicians and Surgeons, Columbia University.

conditions of the Elson-Morgan test, but a considerably more intense color is obtained if sodium hydroxide is used in place of sodium carbonate. Glucosamine, on the other hand, fails to give any test if sodium hydroxide is used.

This test was used in the analysis of clinical preparations of streptomycin. Samples of high purity gave reasonably good results, but as the purity of the samples decreased, the results became high and in some instances were as much as 200–400 per cent higher than those expected from the microbiological assay (see Table 1). It is therefore apparent that interfering substances are present in clinical preparations of low potency.

TABLE 1

COMPARISON OF VALUES OBTAINED ON CLINICAL SAMPLES OF STREPTOMYCIN BY MICROBIOLOGICAL ASSAY (*3*) AND BY THE USE OF THE MODIFIED ELSON-MORGAN TEST

Bio-assay (units/mg.)	Colorimetric assay (units/mg.)	Bio-assay (units/mg.)	Colorimetric assay (units/mg.)
700	750	600	748
705	745	500	700
800	850	390	710
720	725	300	560
750	730	230	900
705	720	115	250
615	600		
770	795		
840	775		

Efforts to remove the interfering substances by selective adsorption methods were made without success. It was observed, however, that the ability of pure streptomycin to give the color test was rapidly lost upon pretreatment with alkaline borate buffer of pH 12 at 100° C. (15.26 grams of $Na_2B_4O_7 \cdot 10H_2O$ and 120 cc. of 1 *N* NaOH diluted to 1 l. with distilled water). The color test of pure streptomycin decreased 90 per cent after 5 minutes, and the destruction was essentially complete after 10 minutes of heating. If a clinical sample of streptomycin of intermediate potency (200–600 units/mg.) is treated under these conditions, destruction proceeds first at a rapid rate approximating that found for pure streptomycin; but after 10 minutes heating, at which time the sample was shown to be devoid of streptomycin activity microbiologically, a second and much slower rate became apparent.

Extrapolation of the rate of destruction of this impurity to zero time permitted estimation of the impurity. The difference of this value and the total value obtained before alkali treatment was expected to correspond to the true streptomycin content of the sample. Values corresponding to the microbiological assay could be obtained on a number of low-potency samples. However, on some samples the values remained high, indicating the presence of other impurities behaving like streptomycin.

The use of the modified Elson-Morgan reaction will give useful results on highly purified streptomycin samples and can be used as a sensitive method for the estimation of N-methyl-l-glucosamine. The differential procedure improved the analytical data obtained with some low-potency samples, but with other samples high analytical values were still obtained.

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Relation of Vapor-Pressure Deficit to Evaporation From a Spherical Atmometer in an Air-conditioned Room

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Ecologists, hygienists, and others interested in the direct measurement of evaporativity by means of the 5-cm. porous-porcelain atmometer sphere are frequently confronted with questions concerning the relation of measured evaporation intensities in calm and shade to air temperature and air humidity, or to vapor-pressure deficit. Of the many different forms of atmometers proposed from time to time under various names and by various writers (*2*), the 5-cm. hollow white porous-porcelain sphere with standardization coefficient of about 0.78 is generally most satisfactory in the absence of frost (*3*). Its moist, spherical surface, without any superficial film of water, gives constant and uniform exposure in all directions excepting below, where the narrow cylindrical neck connects with the supply tube, through which distilled water rises by suction from a reservoir at a convenient lower level. Black spheres are useful when sunshine or other intense radiation requires special consideration.

To care for slight variations in the size of these spheres, each reading is multiplied by the standardization coefficient of the sphere used. When a sphere becomes soiled by dust or other contamination through use, its coefficient generally increases, but it may sometimes decrease, and restandardization is in order whenever considerable soilage is suspected. Soiled spheres may be reconditioned by cleaning; if they are reground, the new coefficient should be slightly greater than the original one.

Although spheres with an original coefficient of about unity (instead of about 0.78) might be produced (external diameter, about 4.4 cm. instead of 5 cm.), the many published evaporativity records based on the 5-cm. instrument render it undesirable to introduce a smaller sphere, exposure of which to sunshine and air currents would naturally differ from that of the 5-cm. sphere in several ways other than with respect to extent of exposed surface.

While the corrected rate of evaporation from a standardized atmometer depends upon prevailing vapor-pressure deficit, air movement, and radiation, rates at stations in calm and shade may be taken to be essentially proportional to the prevailing deficit; under these conditions air movement and radiation effects may be left out of consideration. The value of the deficit, D, at any time may be computed from the current relative humidity, H, and the standard vapor tension, T, for the current temperature, since $D = T\ (1-H)$. But the average value of D for a period is not to be satisfactorily derived from the corresponding average values of T and H unless at least one of them is maintained throughout the period. When both are maintained, the value of the deficit is naturally also constant throughout the period.

This paper reports the result of a 12-month series of weekly observations on the performance of a standardized 5-cm. white atmometer sphere (with coefficient of 0.78), freely exposed under conditions of shade and calm in an indoor storage space with air temperature and relative humidity (and also vapor-pressure deficit) automatically well maintained, at about 70° F., 50 per cent, and 9.29 mm. of mercury column, respectively. The almost constant daily corrected rate of evaporation from the instrument was found to be 15.5 ml., and the ratio of this value to the nearly constant value of the deficit is about 1.668. This new calibration characteristic of the standardized sphere should be essentially correct generally for air conditions of shade and calm, especially indoors, as in homes, offices, and workrooms without considerable radiation or air currents. It may be useful also in comparative studies on outdoor evaporativity.

Our observation period extended from October 1937 to September 1938. The instrument, with bottle reservoir and without nonabsorbing valve (*1*) stood in an air-conditioned storage room in Cleveland, Ohio, kindly placed at our disposal by the National Carbon Company. Each weekly reading was first multiplied by 0.78, the standardization coefficient of the sphere used. From the resulting corrected weekly rates the average corrected daily rate for each of the 12 months, October to September, was then computed as follows: 15.8, 15.7, 14.6, 15.9, 15.4, 16.3, 15.4, 15.0, 15.5, 15.5, 14.8, 16.1 ml./day. For the whole period, the average rate was 15.5 ml./day, or 0.646 ml./hour, and the range of fluctuation from month to month is seen to have been narrow—between extremes of −6 per cent (December) and +4 per cent (September).

Close agreement among the monthly averages constitutes clear evidence that the air-conditioning of this room was remarkably efficient. The automatic temperature and humidity controls were set to maintain air temperature of 70° F. (21.1° C.) and a relative humidity of 50 per cent. Doubtless there was some insensible air circulation at all times, but air movement was not noticeable. Standard vapor tension for 21.1° C. is 18.58 mm. and, since the room air was always about half saturated, the prevailing vapor-pressure deficit was about 9.29 mm. Consequently, the ratio of the value for average daily evaporation rate to that for average deficit is 15.5/9.29, or 1.668. Based on the average hourly rate, this ratio value is 0.0695.

The air temperature of the room used (70° F.) was lower than is usual for artificially heated homes and offices in this country, where 72° F. is often regarded as most satisfactory for the comfort of sedentary occupants. Many short-period tests, carried out at Baltimore with standardized 5-cm. spheres, have indicated that a high degree of winter comfort is often attained in homes and offices with calm air at about 72° F., corrected evaporation rates about 0.75–0.8 ml./hour, humidity about 45–42 per cent, and deficit about 10.8–11.5 mm. To secure such winter conditioning in the region of Maryland, Ohio, etc., artificial humidification of some kind is, of course, generally necessary, especially in periods of coldest weather.

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A Simple, Rapid Technique for the Study of the Action of Hydrolytic Enzymes on Insoluble Substrates

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For the study of the enzymatic digestion of catgut a very simple technique has been used (*1, 2, 4*) for determining the end point of the reaction as indicated by the complete loss of strength of the suture. In this procedure a suitable weight is attached to the suture, which is in turn immersed in the enzyme solution. The falling of the weight resulting from the

rupture of the suture is taken as the end point of digestion. This technique has been made quantitative by Lion and Sizer (*3*), who recorded automatically on telephone-message counters the digestion times of the sutures. The technique has been found to be sufficiently quantitative for use in the study of other fibrous material such as casein, soybean protein, and collagen filaments (*5*).

Since most substrates for enzyme action are not available in the form of filaments, it seemed desirable to adapt this technique to the study of insoluble solid substrates which become soluble upon digestion. It would then be possible to utilize this "breaking time" technique for the study of a wide variety of proteins, carbohydrates, lipids, and other organic compounds. In preliminary experiments this was done by coating a narrow strip (3 mm. wide) of lens paper (Cenco) with a suitable substrate which could be rendered insoluble by heat denaturation or by immersion in some suitable precipitating bath. For example, a lens-paper strip is dipped in 5 per cent egg albumin, dried, then dipped for a few seconds in boiling water to coagulate the protein. After drying the strip a suitable weight[1] is attached and the preparation immersed in a solution of trypsin. This technique was found satisfactory for the qualitative study of the digestion of a number of substrates but usually lacking in satisfactory reproducibility.

An entirely satisfactory method, which was finally devised, is the following: A sheet of lens paper (Cenco) is cut in half. A strip about 1.2 cm. wide along the edge of one piece is painted (using a camel's-hair brush) with a suitable solution or suspension of the desired substrate. The second piece is then placed over the previously painted portion, the edge overlapping by 1.2 cm. The substrate functions as an adhesive in sealing the two pieces together. After drying, the substrate is rendered insoluble by some appropriate technique and the preparation again dried. The lens paper preparation is then cut into 65 strips 2 mm. wide, with the overlap area in the middle of each strip. A colored glass bead is tied to one end of the strip with thread and the preparation immersed in the enzyme solution (see Fig. 1). For short digestion times the falling of the bead to the bottom of the test tube can be detected by eye or ear, but when digestion proceeds slowly, the automatic timing device is preferable.

This coated lens-paper technique is suitable for studying such properties of the enzyme as total activity and the effect of environmental factors such as pH, temperature, oxidation-reduction potential, activators, inhibitors, etc. On the other hand, this technique yields no information concerning the chemical transformation of the substrate induced by the enzyme, except to indicate that the substrate is eventually rendered soluble. In addition to its great simplicity and its reproducibility, the coated lens-paper technique has the advantage that relatively small amounts of substrate are required; with most substrates less than 1 mg. suffices for a single test.

[1] It must be heavy enough to break an uncoated strip of lens paper but not so heavy as to break the coated strip until after digestion of the film has occurred.

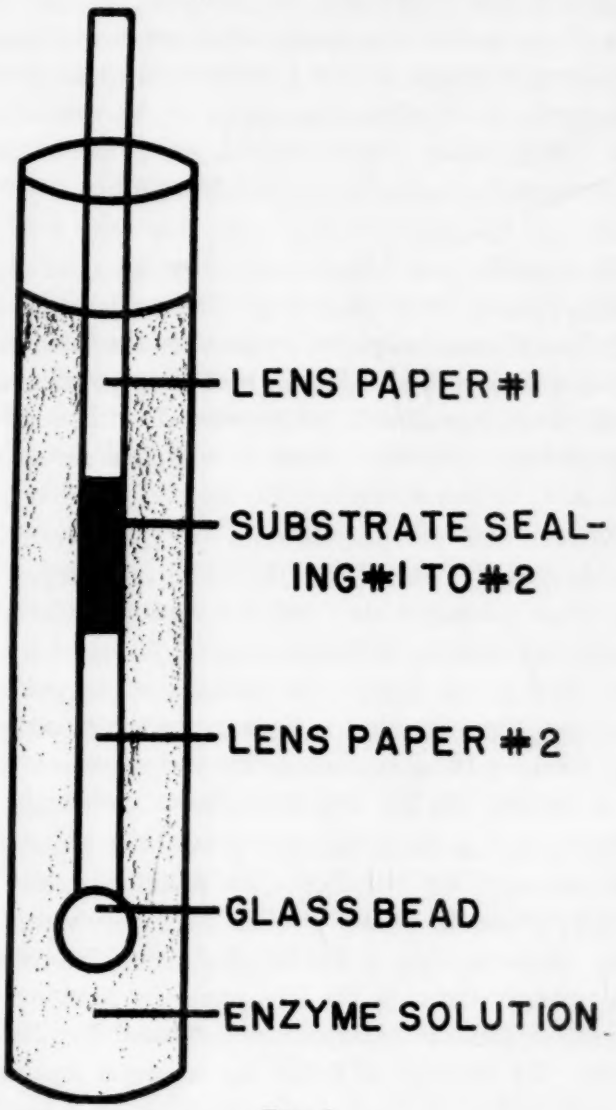

FIG. 1

METHODS AND RESULTS WITH TYPICAL SUBSTRATES

Proteins

Egg albumin. The edge of the lens paper was coated evenly with a saturated solution of egg albumin (Merck), using a camel's-hair brush. The second piece of paper was placed on top of the first with the overlap area 1.5 cm. wide. The coated paper was dipped for a few seconds in boiling water, dried, and then cut into strips. The overlap area of each strip was found to be coated with 0.71 mg. albumin. A 830-mg. glass bead was attached by a thread to each of six strips, which were then immersed in 5 ml. of 2 per cent filtered trypsin (Cenco, final pH 7.0) at

37 ± 0.1° C. Several series were run; in a typical experiment the digestion times were 46, 46, 49, 50, 53, and 53 minutes (average, 49.5).

Globulin. A 5-per cent solution of bovine globulin (Armour) was prepared. The preparation and digestion of the coated lens-paper strips were the same as for albumin except that a 1-per cent trypsin solution was used. Each strip was found to be coated with 0.30 mg. globulin. In a typical series the digestion times were 8, 11, 11, 11, 12, and 15 minutes (average, 11.3).

Hemoglobin. A 2.5-per cent suspension of hemoglobin (Merck) was prepared. The preparation and digestion of the lens-paper strips were the same as for albumin except that 0.5 per cent trypsin was used. Each strip was found to be coated with 0.20 mg. hemoglobin. Digestion times in a typical series were 7, 7, 8, 8, 8, and 9 minutes (average, 7.8).

Casein. A 5-per cent solution of casein (technical) was prepared in 0.1 N NaOH. The lens paper was coated in the usual way and the casein rendered insoluble by washing with 0.1 N HCl followed by distilled water. A 1-per cent solution of trypsin was used for the digestion. Each strip contained 0.40 mg. casein. In a typical series the digestion times were 18, 18, 19, 22, and 23 minutes (average, 20).

Collagen. A dilute collagen gel (about 1 per cent) was prepared by blending with distilled water beef tendon, which had been swollen in 1 per cent acetic acid. After coating in the usual manner, the collagen was precipitated onto the lens paper by washing with saturated sodium bicarbonate followed by distilled water. An average of 0.015 mg. collagen was found on each strip. Typical digestion times by 2 per cent trypsin in a series were 9, 9, 10, 10, 10, and 13 minutes (average, 10.2).

Carbohydrates

Starch. The edge of the lens paper was coated with a boiling, 5-per cent suspension of potato starch (Baker's). Each strip was sealed with 0.43 mg. starch. The amylase used was 1.0 per cent taka-diastase (Parke, Davis, pH 6.9). Typical digestion times of a given series were 3, 3, 3, 4, 4, and 5 minutes (average, 3.7).

Pectinic acid (de-esterified). The coating agent was 2 per cent de-esterified pectinic acid.[2] It was precipitated with $CaCO_3$ followed by washing with distilled water. Each strip was sealed with 0.23 mg. pectinic acid. The digestion was carried out at pH 4.0 (acetate buffer) in 1 per cent pectinase.[3] The following digestion times characterized the series of coated lens-paper strips: 8, 10, 10, 11, 11, and 12 minutes (average, 10.3).

[2] Kindly furnished by Dr. Speiser, Eastern Regional Research Laboratory.

[3] Kindly furnished by the Food Technology Laboratory, M.I.T.

Lipids

Several fats were tried, but oils would not seal the two pieces of lens paper together. On the other hand, very hard fats like tristearin and diglycol stearate were found refractory to enzyme action. Soft fats such as the mixtures present in the commercial products, oleomargarine, Crisco, and Spry, were found very satisfactory.

Spry. Spry was melted and then spread on the overlapped area of the lens papers. Each strip contained 1.30 mg. Spry. Small beads, weighing 427 mg., were employed instead of the usual 830-mg. ones. The enzyme solution was a 10-per cent suspension of steapsin (Eimer and Amend) in phosphate buffer (pH 8.1) containing the detergent, Tween-20 (0.1 per cent). The digestion times were 10, 10, 11, 11, 17, and 17 minutes (average, 12.7).

Methyl stearate. The edges of the lens papers were sealed with hot, liquid methyl stearate, which solidified on cooling. Each strip contained 0.68 mg. stearate. Digestion was carried out in a 2.5-per cent filtered solution of the mold enzyme, keralin (American Cyanamid, pH 5.6). The digestion times were 34, 34, 34, 35, and 43 minutes (average, 36).

Summary

A rapid, simple, quantitative technique has been developed for the study of the action of hydrolytic enzymes on certain insoluble substrates. The end point of digestion is indicated by the release of a glass bead, when two pieces of lens paper sealed together by the substrate separate due to its digestion by the enzyme.

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Method for Making Filters Transmitting the Near Ultraviolet and Absorbing Visual Light

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The development of simple and inexpensive sources for the near ultraviolet light has resulted in great interest in that band of the spectrum that is transmitted by glass. Filters for absorbing the visual light either are of glass, both expensive and limited in size, or are precision gelatin filters that are also quite expensive. Preparation of filters that serve the usual experi-

mental purposes is neither difficult nor expensive and permits variations in transmission that may at times be desirable.

The greater number of dyes, particularly those approximating black, strongly absorb the range that we wish to transmit, but a combination of methylene blue, fuchsin and phosphine, all of which transmit considerably in the near ultraviolet, will make an approximate black. These can be used in a liquid cell, but it is much better to incorporate them in a gelatin film, as they are then fairly stable and very much more convenient.

To make a glass filter the use of old photographic negatives is recommended but not essential. The old gelatin or emulsion may be readily removed with a 1-per cent solution of caustic or half-strength nitric acid. Either method leaves the glass sufficiently clean so that a substratum is not necessary provided the emulsion side is marked and used to receive the new gelatin coating, which is prepared as follows:

Dissolve .4 gram of methylene blue in 100 cc. of hot water to which is added 1 drop of glacial acetic acid. Make a similar solution of fuchsin and phosphine, omitting the acetic acid. Make a 10-per cent solution of gelatin by allowing it to stand until it is swollen, and melt with gentle heat. Add 2 drops of glycerin to each 25 cc. Pipette 10 cc. of the phosphine, 8 cc. of the methylene blue, and 3 cc. of fuchsin into a cylinder, and add 19 cc. of the gelatin. Mix thoroughly and, if necessary, add 1 drop of normal butyl alcohol to break the bubbles. This amount should be flowed over an accurately leveled 8×10 glass and, when gelatin sets, this may be dried in an upright position.

One of these glasses will be sufficient when the fluorescent ultraviolet tubes are used, but it may be desirable to use two, gelatin surfaces face to face, when screening out the visual light from the mercury arc. Visual appearance of fluorescent materials with filters made in this way is comparable to the nickel oxide glass, although the transmission for a given amount of screening the visible light is not quite as good. As commercial dyes were used, it is not expected that the proportions given will produce the most efficient results unless an accurately standardized dye is used. This ratio is based on using Heller and Merz Blue 2 B Dustless, Fuchsin RTN Powder, and Phosphine 3 G 100 per cent. Of course, dyes of other manufacture can be used, and the variation can be adjusted by altering the proportions. Visually, these filters almost screen out an illuminated white cloud with a residual color of deep red, modified by a slight blue transmission. Very thin layers appear to be a rusty gray.

By doubling the concentration of the gelatin and correspondingly increasing the glycerin, it is possible to strip the film from the glass if desired. By treating plate glass with a silicone stopcock grease and polishing off the last visible trace, the gelatin film can be easily stripped merely by cutting around the margins of the plate of glass. In this way the transmission can be extended further into the ultraviolet that would be absorbed by glass.

Letters to the Editor

Some Notes on the Cancer Problem

In writing the following lines of comment on K. S. Pilcher's letter (*Science*, 1946, **104**, 167) concerning an organized attack on the cancer problem, I wish to acknowledge his well-done, traditionally constituted argument for a coordinated, well-financed research program. Certainly I do not wish to argue against a program of such highly important and humanitarian purpose. I merely wish to point out a point of view which, in my opinion, may not be basically correct.

The argument for a planned and completely coordinated cancer program on a national scale is based on the rapid results obtained in the fields of atomic fission, penicillin and other antibiotics, etc. by means of highly coordinated research efforts. However, an examination of the background of these problems shows that the rapid practical evolution was really in the region defined as "development" rather than "research" or "discovery." Thus, the rapid development of the atomic explosive was subject to the fortuitous discovery of the fission of a particular nucleus under a particular treatment, the fission occurring in a particularly desirable manner. I believe that I am correct in saying that the fundamental idea of a self-perpetuating atomic fission chain is relatively old, including the general ideas of power generation and the causation of explosive decomposition. That is to say, the principle of generation of such a reaction was seen to lie in finding a nucleus capable of producing enough of the right kind of secondary particles to carry on the chain. On the basis of knowledge in the 1930's, the finding of such a nucleus may well be called fortuitous. In the case of penicillin, too, I believe that it is correct to say that it was essentially chance that the particular conditions were accumulated simultaneously to show the antibiotic effect in a spectacular manner; once the goal was seen, the mass-development of the processes, etc. was a foregone conclusion.

However, in a field in which no clearly defined line of approach can be said to exist, it is quite doubtful that a rigidly planned program would produce results more

rapidly than the time-honored method of "independent groups." The difficulty of a planned program in such an instance is obvious: a considerable concentration on much detail in relatively few directions. The probability of hitting the correct solution would depend simply on having one of these few directions coincide with a particular, a right, method of approach. Looked at in this manner, the probability of hitting the correct solution is not very good.

While I am by no means a specialist on the cancer problem, I feel that it is justifiable to say that as yet we do not have a clear-cut line of approach to the solution. We are still irradiating with electromagnetic energy and with radioactive materials, we are still using surgery, etc.; in a word, we are doing much the same things that were being done years ago, in the factual sense of the word. To be even more specific, I would say that we are still completely at a loss, and that no one can predict which of the many branches of the physical science will eventually lead to the answer. While the promising lines should be pushed by sheer "man-hours," there must be at least a corresponding support of the "individual groups" which, not being tied to a definite approach, would have, in my opinion, a greater chance of indicating the right direction to be followed by the mass-effort, which would not be too difficult to finance once the probability of success begins to approach unity.

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On the Theory of Acids and Bases

There is one theory in our biochemical and biological sciences that needs drastic revision, and that is the idea of acids and bases.

It seems to me that we should accept the theory that an acid is "anything" (ions, molecules, or particles) that yields hydrogen ions and that a base is "anything" that combines with hydrogen ions. This would get rid of the idea, for example, that a sodium ion is a base and brings forth the idea that such ions have other functions in the animal body, such as irritability and osmotic pressure regulations.

Many biochemists and biologists say that a food is basic in reaction because it contains sodium. This seems incorrect, because the negative ion should be considered the base. For example, if one takes sodium citrate into the body, the citrate ion is the base which, when oxidized, yields the bicarbonate ion, one of the most important bases of the blood. Vegetables are basic forming foods because they produce bicarbonate ions. The production of such a base takes place because there must be as many negative as there are positive ions, and when carbon compounds are oxidized in the body, they will yield bicarbonate ions if there is a positive ion with which to combine; otherwise, the $HHCO_3$ formed is eliminated as CO_2 and H_2O. When a chloride or sulfate ion, as in table salt, is already present in the food, the $HHCO_3$ is also eliminated as stated above.

The theory that the kidney functions in acid-base balance because it retains sodium when the acids are formed in the body is out of date. It seems more logical to say that ammonia is formed in the kidney which combines with the acid to be excreted, so that the body does not deprive itself of the sodium needed for osmotic pressure and nerve regulations and in order that the bicarbonate ion (alkali reserve) will not be used up. For example, we can show:

$$\underset{\text{base}}{2\,Na^{+} + 2HCO_3^{-}} + \underset{\text{strong acid}}{H_2SO_4} \rightarrow \underset{\text{very weak base}}{2\,Na^{+} + SO_4^{--}} + \underset{\text{weak acid}}{2H_2CO_3}$$

$$H_2CO_3 + \underset{\text{base}}{K^{+} + Hb^{-}} \rightleftarrows \underset{\text{weak acid}}{HHb} + \underset{\text{base}}{K^{+} + HCO_3^{-}}$$

$H_2CO_3 \rightleftarrows CO_2 + H_2O$ or to prevent loss of alkali reserve,

$$\underset{\text{base}}{2\,NH_3} + \underset{\text{strong acid}}{H_2SO_4} \rightarrow \underset{\text{weak acid}}{2\,NH_4^{+}} + \underset{\text{very weak base}}{SO_4^{--}}$$

$$\text{Organic acid} \xrightarrow{(o)} CO_2 + H_2O$$

is therefore not acid in reaction when metabolized in the body. Why say the potassium or sodium ion is a base when it does not enter into the reactions?

It should be made clear that meats act acidic in the body because when they are metabolized they form H_2SO_4 and H_3PO_4, which are strong acids and must be neutralized. Sodium chloride and sodium sulfate are not basic, because the chloride and sulfate ion are very weak bases, while monoacid phosphate and bicarbonate ions are rather strong bases. Why can't such ideas be used in the explanation of acid-base balance in the animal body? This would get rid of the ridiculous idea that a sodium ion is a base.

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Injection vs. Oral Administration of Folic Acid in the Chick

Previous experiments (D. V. Frost, F. P. Dann, and F. C. McIntire. *Proc. Soc. exp. Biol. Med.*, 1946, 61, 65) indicated that 10 μg. daily of synthetic folic acid (*L. casei* factor, kindly supplied by Lederle Laboratories and identified as pteroyl glutamic acid) was sufficient to produce good growth, normal feathering, and near-normal pigmentation in chicks over an 8-week period when the material was given by intramuscular injection. When 10 μg. daily of folic acid was given orally under similar conditions, growth, feathering, and pigmentation were relatively poor. At levels of 2.5 and 5 μg. daily of folic acid there was an equally marked difference in the response between injection and oral administration. The following experiment was set up to resolve clearly the question whether synthetic folic acid was more active by injection than when given by mouth.

Synthetic folic acid, 200 μg./cc., was dissolved with trace of ammonium hydroxide at pH 7.0. Benzyl alcohol, 1.5 per cent, was added, and the solution was sterilized by filtration and filled into vials. The potency of

TABLE 1

Group	Folic acid per chick per day γ	No. of chicks Started	No. of chicks Surviving	4 weeks Body wt. (grams)	4 weeks Feathering	8 weeks Body wt. (grams)	8 weeks Feathering
Injected subcutaneously	2.5	10	9	204	Poor	362	Poor
	5.0	7	6	242	Subnormal	492	Subnormal
	10.0	8	8	243	Normal	517	Normal
Given orally by pipette	5	10	8	183	Poor	279	Poor
	10	8	7	244	Poor	405	Subnormal
	20	8	5	234	Poor	569	Subnormal

the solution was standardized by microbiological assay using *L. casei* and was checked twice during the assay period. Day-old Black Leghorn chicks were fed the basal diet previously described (*Proc. Soc. exp. Biol. Med.*, 1946, **61**, 65). The chicks were divided into 6 groups of 8. Three of the groups were given dilution aliquots of the folic acid solution orally by pipette in amounts of 5, 10, and 20 μg./day. The remaining three groups were given similar dilutions by intramuscular injection at levels of 2.5, 5, and 10 μg./day. The data are shown in Table 1.

These data indicate that folic acid is approximately twice as effective by injection in chicks as when given orally. Campbell, Brown, and Emmett (*J. biol. Chem.*, 1944, **154**, 721) concluded from a somewhat similar experiment of 4-week duration that the two forms of administration have the same biological effect. Analysis of their data shows that folic acid by subcutaneous injection actually evoked a slightly greater response both in the weight gain and hematopoiesis than did the same amounts given orally. As seen in the above table, the difference in growth response between the two forms of administration is accentuated to a clearly noticeable degree in the longer period of our study. There was also a higher survival among the animals receiving folic acid by injection in both sets of experiments.

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Book Reviews

An outline of organic nitrogen compounds. Ed. F. Degering and collaborators. Ypsilanti, Mich.: University Lithoprinters, 1945. Pp. vi + 752. $7.50.

This book, which is a revision and enlargement of the previous (1942) planographed edition, covers in outline form many of the more important types of open-chain organic nitrogen compounds and, to a lesser extent, heterocyclic nitrogen compounds. Its scope is indicated by the following list of topics treated in 45 chapters: a chronological survey, general concepts of structure, nitrogen fixation, the ammonia system of compounds, aliphatic nitro compounds (5 chapters), aromatic nitro compounds, nitroso compounds, oximes, aliphatic and aromatic amines, amino acids, polypeptides, proteins, aliphatic diazo compounds (diazenes) and azides (triazenes), aromatic diazo compounds, azoxy compounds, derivatives of hydrazine, urea, thiourea, guanidine, sulfamic acid and sulfamide, amides, imides, nitriles, carbylamines, isocyanates, cyanogen and related compounds, organic nitrogen dyes, alkaloids, medicinals and vitamins containing nitrogen, high polymers containing nitrogen, pyridine, quinoline and the synthesis of nitrogen ring compounds, explosives, some miscellaneous nitrogen compounds, and isomerism of organic nitrogen compounds.

The extent of treatment of these topics varies from fairly comprehensive in certain cases (for example, aliphatic and aromatic nitro compounds, amines, oximes) to very brief in others (proteins, polypeptides, alkaloids, polymers containing nitrogen). The material is presented in outline form, usually under the following main headings: (a) history, occurrence, structure, and uses; (b) nomenclature; (c) preparation; (d) physical properties of some examples; and (e) reactions. Although the outline form permits the presentation of a maximum amount of material in the allotted space, it also tends to obscure the relative importance of various methods of preparation and the degree of usefulness of the reactions. In some cases an evaluation by the author partially offsets this, but a wider inclusion of yields, where available, would have been helpful from this standpoint and would have enhanced the value of the work as a reference book.

For the most part the presentation of material is clear and concise, with the inclusion of equations and formulas. In places, however, the treatment is so condensed or cursory as to give the student little insight into the nature of the reactions. Thus, the treatment of the Arndt-Eistert reaction (p. 270) would leave the student at a loss to know how (or if) the first step could be controlled to give a diazoketone instead of a chloroketone, how the rearrangement step is carried out and the need for a catalyst, and gives no indication of the value of the reaction. The brief mention of the Bucherer reaction (p. 294) also is unenlightening. In neither case is reference given to the reviews in "Organic Reactions." Other examples might be cited.

Nevertheless, the book should be of value as an organ-

ized, although not too critical, compilation of reactions with extensive references (over 5,200) to the literature. There is a good index, referring to paragraphs, which makes the material in the book readily accessible.

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Mammals of Nevada. **E. Raymond Hall. Berkeley-Los Angeles: Univ. California Press, 1946. Pp. xi+710. (Illustrated.) $7.50.**

This product of 35 years of field and museum work began with Miss Annie M. Alexander's trip of 1909. For a third of a century Nevada was one of the training grounds of some 60 or 70 students and staff from Berkeley. This contemporary remembers Miss Alexander's wise choice of Jordan's student, Joseph Grinnell, and does not think of the Museum without the triumvirate of Grinnell, Dixon, and Hall coming to mind.

Seventeen thousand eight hundred sixty-one Nevada (15,000+ in M.V.Z.) specimens were examined, and "232 kinds (species and subspecies) of 111 full species which belong to 57 genera of 23 families of 6 orders" are treated. The treatment of each subspecies is under six headings: scientific name, common name, synonymy, distribution, remarks (measurements, weight, related forms), and records of occurrence. Under species the author gives notes on color, trapping, pelages, reproduction, size, habitat, habits, and other ecological items. Some species have extended accounts, such as the badger (10 pp.), coyotes (22 pp., including trapping, control, control methods, why control, alleged gains and losses, facts, personal views, suggested plan), townsend ground squirrel (10 pp., including Alcorn's work), black-tailed deer (9 pp.), and striped skunk (10 pp.). Occasionally this account appears under the genus, as in the case of the pocket gopher, *Thomomys* (13 pp.).

The book contains 81 large distributional Nevada maps (with N.A. insets), 11 full-page fine representative habitats, 470 skull and tooth figures and 15 other figures (8 of which are maps of relief, precipitation, life zones, faunal areas and center of differentiation, Lake Lahontan, type localities, counties), and the customary appreciated colored life-zone chart of former Museum publications. Factors responsible for geographic distribution as given by the author, are: edaphic factors, plants, moisture, number of mammals (20 per acre), fluctuations in Lake Lahontan (pre- and post-populations), cline gradients of size, etc., speciation (e.g. 4 species or 29 subspecies of *Thomomys,* pocket gopher, or 9 species and 13 subspecies of *Eutamias,* chipmunk), and desert character of mammalian fauna. Usually the subspecies are ecologically in distinct habitats, but in Nevada, as elsewhere, there are puzzling overlaps. There is a convenient check list and classification schema of Nevadan mammals and a well-planned key to genera and species. The illustrations (copies) should have the customary "after ——." The book closes with a hypothetical list, appropriate map and list of type localities, gazetteer, glossary, literature, and index. The gazetteer (23 pp.), like those of Linsdale, is very helpful.

This volume's author, sponsors, and press are to be congratulated on this handsome book and its excellent format. Not even the most populous state can claim such a thoroughgoing, extensive account of its mammal fauna. It is a standard, set by one of the best living authorities on North American mammalogy, which future students of western mammals will use constantly.

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Scientific Book Register

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